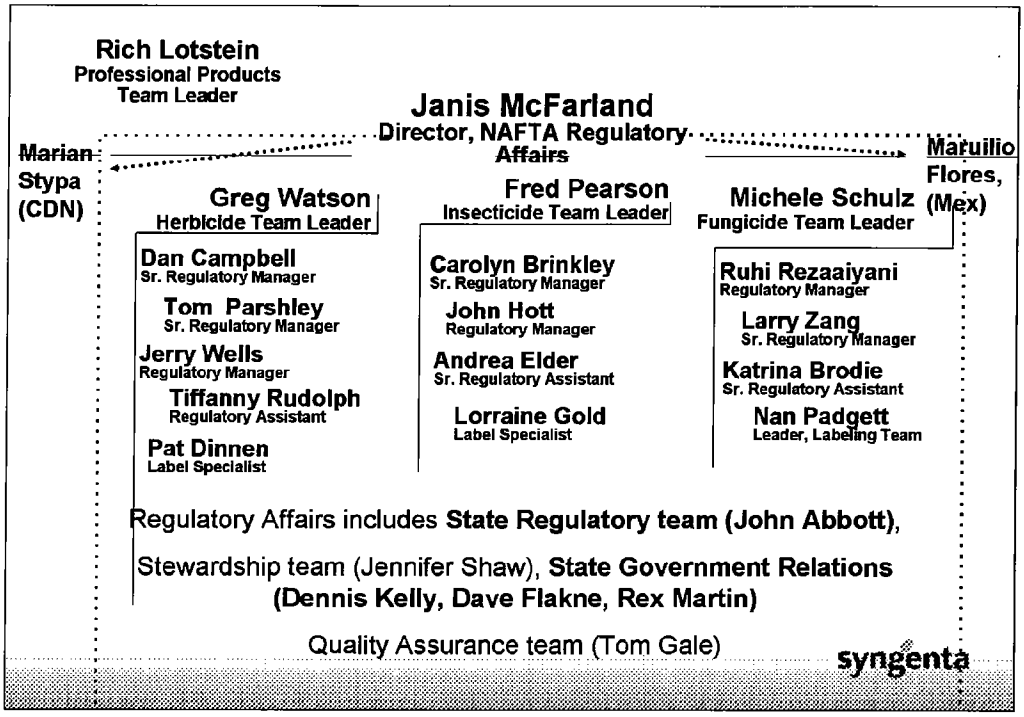

Mention folks not wanting to move to GSO, limited Zeneca knowledge transfer

Herbicide Regulatory Affairs - General

- **Regulatory affairs is a sales job**
  - We sell data and decisions
- **Regulatory affairs is a mixture of science and politics**
  - Have to excel in both to succeed
- **Regulatory strategy is a component or an extension of the marketing strategy**
  - Important that the marketing / regulatory strategy is coherent
- **Herbicide 'Market Creation' Team Goals:**
  - To be & to be recognized as 'Best in Class'
  - Successfully defend existing registrations (high importance given state of active ingredient development pipeline)
  - Deliver on-time, full quality / freedom to sell new registrations

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Herbicide Regulatory Affairs - General

- Doing 'NAFTA' within PMT structure, no regional coordination specific positions
- Current Active Ingredient Load 2X Industry Average (24 AI's, ~ 100 registrations)
  - Global Herbicide Reg: 10 mgrs, 2 assistants; EU Herbicide Reg HQ: 8 mgrs, 1 assistant (does NOT include country reg)
- Globally - work with Regulatory Development Teams to feed into the Global Product Leadership Team
  - Excellent working relationship with Corn PLT, Extremely limited linkage with other PLTs
  - Global holds the development budget, have to work internally for NAFTA share
- HAES resource within NAFTA key to our regulatory success, HAES is sort of like the Regulatory Supply Chain!
  - Relationship building with EPA / PMRA (i.e., over 200 people each in EFED / HED)
  - Resource not available to fully support the current portfolio (small to mid-size products at risk)
  - Separation of key science facilities ICTL & JH in UK) from Regulatory & Business a concern

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Regulatory Affairs - Inerts

Use of an inert in a end-use product for a food use requires either establishment of a tolerance / MRL or an exemption from the requirement of a tolerance

Non-food use inerts do not require a tolerance but review & approval by EPA for such a use

As FIFRA is an 'intent' statue, inerts do not require registration. For example, herbicide safeners require data packages roughly equivalent to that of an pesticide AI but they still are not registered.

FQPA required review of all existing tolerances / exemption from tolerances by 2006 – including inerts

Will have a dramatic effect on inerts available for use in Crop Protection

Inerts will likely be included in Endocrine Priority Screening program

- Again may result in inerts being withdrawn from pesticide market by suppliers

Data compensation proposal – EPA has proposed a data compensation scheme akin to the one in place for AI's.

- Will discontinue allowing change of inert suppliers by notification
- Estimated only 8 – 10 inerts have data subject to compensation at this point in time (includes safeners)

CDN PMRA moving to ask industry to eliminate nonyl phenol in end-use products

- Driven by Environment Canada, not PMRA
- Moving ahead of EPA tolerance reassessment process, even though PMRA uses EPA approved inert list

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Short Overview – Blockbuster AI's

● Paraquat

RED under FQPA in 1997; need to resolve approved label with tolerances. Need to prepare to pay fee to move this petition, wheat harvest aid forward.

AWT project a critical development

Important threat coming from medical research in USA; pushing for market basket survey, water monitoring in 2004 to prove 'near zero exposure' of general population to paraquat; remove hops & potatoes from label.

Third party registration application may be imminent

● Mesotrione

Sweet corn approval

Carryover; Cu form = mesotrione acid??, new formulation development

CuOH tolerance exemption needed

Production issues including Ames testing of technical

PGW site approved, initiate small water monitoring program in 2005/6

● Clodinafop/cloquintocet

US: Conditional EPA registration in 2000, with many data gaps, led to 4% sales cap, annual renewal of registration, 'likely human carcinogen', and geographical restrictions.

Submission made in May 2003 fulfilling all data gaps and petitioned for:

Refuting oncogenicity classification, Removal of sales cap and conditional registration, Allow for full section 3 label with no geographical restrictions

Push to get this on the 2004 workplan was not successful; Currently Syngenta's #3 company review priority (fee system may allow for review timeline of 18-22 months).

Canada: PMRA notified Syngenta of a special review (due to unfavorable conclusions from EPA) - not followed through by Authorities to date. Data generated as part of EPA conditional submission gives us fairly good chance of maintaining business through a re-review, should this ever be acted on by PMRA.

● S-MOC/benoxacor

TRED under FQPA in 2001; need to copy all tolerances to S-MOC section of 40 CFR § 180.368

Acetochlor review could re-open common mechanism of toxicity question (particularly for metabolites)

Third party registrations / lawsuit pending vs. EPA

Regulatory threat from metabolites in water & from states in upper Midwest

Need to amend benoxacor tolerance to reflect S-MOC tolerances

Endangered species

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Short Overview – Growth AI's

- **Glyphosate**
  - Endangered species, increased detection of water residues
  - Resistance management PR notice
- **Fluazifop-p-butyl**
  - TRED in progress, completed in 2004/5; issued a management warning on the outcome

Rich Text Format

  - Issues are bridging data to racemate, hamster study instead of a mouse as EPA requested, hamster study has oncogenic response, database shows reproductive effects so FQPA additional 10X will be applied followed by Prop 65 classification
- **Trifloxysulfuron-sodium**
  - Very minimal outstanding data gaps from initial registration
  - Endangered species
  - Need to sell in tomatoes for political reasons
  - Need to monitor use in sugar cane in FL (given atrazine issues in vegetables)
- **NOA 407855**

US/Canada: Submission January 31, 2004 as joint review, reduced risk candidate with full electronic submission = highest priority review category for EPA / PMRA.

Key Success Factor: Achieve reduced risk, expedited review status gives potential for 2ndQ 2006 registration.

Threats: Marginal increase in lung tumors in mouse lungs: Believed to be caused by ingress of test material into lungs, as an artefact of gavage dosing procedure. Key investigative work being performed to prove this is a localized, non-systemic effect, which is not relevant to workers via inhalation route of exposure.

Dietary Carcinogenicity study being conducted as backup (key data available July 2004, final report Oct 2004). Other toxicology issues felt to be manageable at this time

EPA Fee system could lengthen timeline, though registration in time for full 2007 launch would still be possible.

If RR not achieved, will realize improvements in timeline through Joint Review/ Electronic submission timeline. Potential for ~2ndQ 2007 registration.

Worst case: EPA/PMRA will not accept package until backup dietary Carcinogenicity study complete. Potential for late 2007 – 2008 registration.

Other: End-use products – Currently plan to submit A12303C as lead candidate; A12303D is backup (addresses potential worker exposure challenges with "C"). Additionally registering an adjuvant and expanding tolerance for safener in US.

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What we can do for you?

- Defend current sales
- Consistent delivery of registration timelines / targets
- Provide input / guidance / predicted outcomes on development / marketing strategies
- Deal with questions on labeling, 'mistakes' in manufacturing
- Provide competitive advantage particularly for third party registrations involving Syngenta active ingredients
- Provide competitive analysis (quality & timing of registration, predict outcomes)

What we need from you?

- ~~Priority – what should we work on & what should we defend?~~
- Support of our needs locally / globally (based on market need)
  - Reduced risk documents, labeling comments, label DFU's, efficacy data for CA submissions, initiate studies, resource allocation, etc.
- Ability to influence / provide input into marketing strategy
- A partnership!!

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Ways of Working

- ~~Suggest retention of Core PMT concept to manage Brands / Active ingredients~~
  - Brand Mgr, Technical Brand Mgr, Regulatory Affairs Mgr, Development Mgr
- Suggest scheduling formal Core PMT Meetings in advance of NAFTA PMT Meetings in Feb 2004
- Need to consciously & consistently work to overcome location differences
  - Informal exchanges will be what is lost
- Need to represent NAFTA, send consistent messages to global

Dan Campbell (336 632 7627)

➢ Mesotrione	Callisto, s-metolachlor (+/- atrazine) +benoxacor+mesotrione, mesotrione+acetachlor	ZA1296
➢ clodinofop	Discover (Horizon, Topik)	CGA-184927
➢ cloquintocet -methyl	clodinofop safner	CGA-185072
➢ Fluazifop-p-butyl	Fusilade, Fusion (fluazifop + fenoxaprop)	
➢ fluazifop+fomesafen	Typhoon	(Share with Tom)
➢ New cereal herbicide	NOA 407 855	
➢ primisulfuron	Beacon	CGA-136872
➢ prosulfuron	Peak, Exceed/Spirit (primisulfuron+prosulfuron)	CGA-152005
➢ Tralkoxydim	Achieve	
➢ trisulfuron	Amber (Logran)	CGA-131036

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Tom Parshley (336 632 7207)

~~➢ ametryn~~	~~Evik~~	~~G-34162~~
➢ atrazine	Aatrex	G-30027
➢ trifloxysulfuron		
➢ dicamba	Vanquish/Northstar/Rave (triasulfuron+dicamba), Target (dicamba+MCPA+mecoprop)	
➢ Fomesafen	Flexstar, Reflex	
➢ fluazifop+fomesafen	Typhoon	(Share with Dan)
➢ norflurazon	Solicam / Zorial / Evital	SAN9789H
➢ prometryn	Caparol	G-34161
➢ pyridate	Tough	SAN319H
➢ simazine	Princep	G-27692

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Jerry Wells (336 632 6324)

➢ butafenacil		CGA-276854
➢ Diquat		
➢ glyphosate (Sulfosate / Glyph trimesium, Glyphosate acid)	Touchdown	
➢ Paraquat	Gramoxone	
➢ Molinate	Ordram (Ordram 15G, Ordram 15GM; Arrosolo [molinate + propanil])	

Rich Lotstein	Barricade, Endurance,
➢ prodiamine	Factor

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Greg Watson (336 632 2993, mobile 336 707 7162)

➢ S-metolachlor	Dual II Magnum, Medal, Bicep / Primextra, Boundary, Expert	CGA-77102
➢ benoxacor	S-MOC Safener	CGA-154281
➢ Triazine support		
➢ R-29148 (Safener)	EPTC safener	

Key Herbicide Regulatory Achievements - 2003

- **Trifloxysulfuron / Envoke & Monument (CH_3Br replacement)**
  - Registration in cotton, sugarcane, almonds, turf, citrus, tomatoes
- **Butafenacil / Inspire (OPa)**
  - Cotton defoliant
- **Mesotrione / Callisto**
  - Popcorn use registered
  - Monthey site / 1st Ames submission completed
  - PGW EPA rebuttal concluded, site selection / characterization accepted by EPA
  - Work on copper salt planned and begun in HAES and PC
  - Supported carryover research, strategy for regulatory approach
  - Supported mesotrione submission in Mexico

First time in Syngenta history two new AI's registered on the same day!

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Key Herbicide Regulatory Achievements - 2003

- **Lumax**
  - Alternate formulation registered, business critical for 2004!!
- **S-metolachlor / Dual MAGNUM**
  - Obtained expanded use registrations / tolerances grasses for seed, sunflower, sugar beet, tomato, spinach
  - Obtained expanded use tolerances asparagus, carrots, horseradish, green onions, rhubarb, swiss chard (will allow for 3 additional years of exclusive use)
  - Continued defense vs. third party metolachlor
  - Boundary 6.5EC new formulation registered
- **Atrazine / Aatrex, Bicep, Lumax, etc,**
  - Obtained successful conclusion of atrazine Jan / Oct IRED, two SAPs, large NGO pressure - despite EU withdrawal from Annex I
- **Molinate / Ordram**
  - Negotiated 5 year phase out, avoided unfavorable RED loss of use in CA

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Key Herbicide Regulatory Achievements - 2003

- **~~Tralkoxydim / Achieve~~**
  - **Tolerances extended until 2005**
  - **Label amendment approved to allow use of conditioner**
- **Clodinafop / Discover**
  - **Submitted > 70 studies required for conditional registration of Clodinafop (submission included all elements needed to refute as many findings as possible, and targeted to support Canadian business)**
  - **New formulation Discover NG registered**
  - **Annual renewal of registration approval**
- **Glyphosate / Touchdown**
  - **Touchdown CF new formulation registered**
  - **Touchdown Pro use expansion approved**
  - **Touchdown Total (K based, resistance management language) new formulation registered**
  - **Registered Huddersfield as production site for technical**

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Key Herbicide Regulatory Achievements - 2003

- **Paraquat**
  - **Developed program to prove low level of exposure (food & water monitoring)**
  - **Submitted leaf alcohol tolerance exemption, got this on 2004 workplan**
  - **Successfully resolved Surefire manufacturing issue**
- **Supported Divestments**
  - **EPTC, napropamide**

Key Herbicide Regulatory Achievements - 2003

- **Primisulfuron TRED completed**
- **SMART Meetings, initiate TRED / RED Process**
  - **Ametryn**
    - Determined which crops we would support in the RED
    - Supporting business licensing effort
  - **Fluazifop-p-butyl**
    - SRRD contacts made for TRED, SMART meeting held. Use Closure memo will be complete by end Nov.
    - Large tox submission and EFED submissions made to prepare for TRED; work on Tox/risk assessment meeting continuing to try to protect current business
    - internal 'alerts' communicated to ensure company-wide knowledge of issues expected out of TRED.
    - CSF / impurity profile issue addressed with 6(a)2 and PC volume submission by end Nov

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Key Herbicide Regulatory Achievements - 2003

- **NOA 407855 Submission Preparation**
  - NAFTA Joint review (with Canada) submission in preparation for Jan 2004
  - First full electronic submission for submission
  - Designed possible pathway forward for Reduced Risk lung results

- **NOA 449480 Business Decision**
  - Supported decision NOT to promote

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Short Overview – Core AI's / Atrazine

- Jan / Oct IRED completed successfully; new MOA expected ~~soon. Cumulative assessment to follow (2005)~~
- Favorable water limit established 37.5 ppb (90-day rolling avg. for TCT in raw water) as targets for watersheds needing mitigation. Eight CWS identified that only get one more "strike" at this trigger; if exceed then use banned in that CWS.
- Other watersheds prioritized and top ~140 will be more intensively monitored starting in 2004.
- Process to mitigate & ban in watersheds, as necessary based on limits (favorable limits, expect limited impact)
- Agreed to establish publicly available Atrazine Watershed Information Center (AWIC) and Hotline to house results, guidance (www.atrazine-watershed.info)(1-866-365-3014)
- Process to eliminate watersheds from future monitoring if 5 years monitoring shows no exceedence (i.e. sunset clause)
- Required to development BMP / mitigation plans for 8 CWS by August 03 & communicate to EPA how they will be communicated to the growers (DONE)
- Rural Well monitoring required due to EPA uncertainties in knowledge; rural well monitoring program still not finally defined
- Costs for water monitoring / other studies to be shared with other registrants as EPA will issue a Data call-in
  - Have opened discussions with other firms for establishing a task force. Likely not to succeed as Syngenta will not accept splitting costs by market share %
- Epidemiological studies regarding atrazine's potential link to cancer do not alter that conclusion that there is a ~~reasonable certainty of no harm from exposure to~~ atrazine so far as cancer risk is concerned. New SAP on cancer will be convened.
- Addition work with frogs will be required, included in DCI
- Ecotoxicological based water monitoring program will include 40 sites, with additional work on modeling. Important to link with Aquatic Life Criteria TMDL from EPA's Office of Water
- Registrants required to voluntarily cancel existing technical registrations (in order to harmonize all atrazine registrations to Syngenta use rates), request new registrations
- Voluntary cancellation of technical registration is contingent on approval of new technical registration
- No product recall, use supplemental labeling & sticker (a la WPS) to cover existing stock
- Labeling for end-use products will require amendment, not cancellation of registration
- Non-restricted use (<4% atrazine) products for homeowner market will not be held to this same schedule or label statements
- Required to have new registrations on new production by April 1, 2004??
- Critical for Syngenta to get EPA to require OTP of other tech registrants for new registrations, opening the door for FIFRA based data compensation arbitration (team currently thinking of linking with MOC arbitration)

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Short Overview – Core AI's

- **Diquat**

TRED completed 2002; no major outstanding regulatory issues.

Zero day PHI for water will require data generation / review

- **Fomesafen**

TRED anticipated prior to 2006; Syngenta asked for TRED to begin in 2004 – believed best pathway to get dry / snap bean, cotton new uses as SRRD actions more likely to undertake policy calls like peroxisome proliferation MOA & relevance to humans

Toxicology data review and oncogenicity reclassification to support new uses in minor crops; EPA SAP driven by ILSI work on peroxisome proliferation being held in Dec 2003.

HED assessment of residue data also needs review

- **Molinate**

Negotiated 5 year phase out (3 years 100% at 2002 volumes, 75% in 2007 and 50% 2008)

Will need to respond to PANNA, NRDC comments to phase out arrangement but only do this to bolster EPA; do not anticipate EPA will change the arrangement

- **Triasulfuron**

TRED expected prior to 2006; no major regulatory issues anticipated

- **Tralkoxydim**

US: Conditional registration in 1996 with 'likely human carcinogen' classification.

All studies submitted to fulfil conditions of registration in 2002. Tolerance and registration expiration date extended by EPA until May 2005 while EPA reviews conditional data. Successful reversal of oncogenicity classification deemed not likely and is not being pursued at this time.

Canada: No issues with registration, which is being protected to avoid the situation that occurred with clodinafop.

Other: End-use products: Achieve SC with additional bottle of 'Morwet' registered for use in both US and Canada for 2004 season; built-in formulation being evaluated for 2005.

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Short Overview - Supplementary AI's

- **Ametryn**

RED underway, completed in 2004/5. No major regulatory challenges anticipated.

AI sales low, will not support substantial investment

- **Norflurazon**

TRED completed in 2002. No major regulatory issues anticipated

Need import tolerances in citrus export receiving companies

- **Primisulfuron**

TRED completed in 2003. No major regulatory issues anticipated

- **Prometryn**

TRED may be initiated in 2004. No major regulatory issues anticipated

- **Prosulfuron**

Tolerances have lapsed, trying to get this inserted into the EPA work plan in 2004. Has led to dropping of registration in Mexico, put us at risk in USA

TRED expected prior to 2006; no major regulatory issues anticipated

- **Simazine**

Cumulative toxicity assessment for all chlorotriazines, anticipated to be part of IRED for simazine in 2005

Will need import tolerances established in EU to support US uses

NAFTA Herbicide Regulatory Team

- ~~2003 Commitments:~~
  - Dan: Microsoft Word Document
  - Tom: Microsoft Word Document
  - Jerry: Microsoft Word Document
  - Greg: Microsoft Word Document

EPA Work Plan

- The work plan for FY 2004 has been released; however, please note that if a fee system comes to the US that will remain as valid (i.e., will be worked on to achieve a registration decision in FY 2004):
  - only the IR-4 actions listed in the New Use table,
  - carry over actions from 2003,
  - and the new inert portion of the work plan

- At the front of the attached document I have extracted the EPA work plan for FY 2004 that is relevant for herbicide & those items that involve Syngenta active ingredients. Good news for us obviously is the inclusion of the mesotrione sweet corn (EPA in error did not list this as a 2003 carryover), the S-MOC IR-4 actions (we accelerated this by 1 yr minimum), and the CuOH & leaf alcohol on the inert work plan. Disappointments for us include clodinafop, the proposed fomesafen TRED, and paraquat wheat harvest aid. Also, we need to dig a bit more on the prosulfuron situation, as last year EPA did have a plan to work on re-establishment of tolerances for both prosulfuron & tralkoxydim that was not listed on the work plan (recall the tralkoxydim tolerances were re-established).
- Again, fees will change the game & the work plan (except for the items mentioned above)

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Overview Documents

- ~~Activities expected at EPA in 2004:~~

- Short overview of Herbicide Active ingredients: